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EXAMINER
JOHNSTON, PHILLIP A

ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 07/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,211	SHIOKAWA, YOSHIRO	
	Examiner	Art Unit	
	Phillip A Johnston	2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Examiners Response to Arguments

1. Newly added Claims 15-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,111,250 to Thomson.

Thomson (250) discloses that in a quadrupole mass spectrometer, typically one of the rod sets is constructed to create an axial field, e.g. a DC axial field, thereon. The axial field can be created by tapering the rods, or arranging the rods at angles with respect to each other, or segmenting the rods, or by providing a segmented case around the rods, or by providing resistively coated or segmented auxiliary rods, or by providing a set of conductive metal bands spaced along each rod with a resistive coating between the bands, or by forming each rod as a tube with a resistive exterior coating and a conductive inner coating, or by other appropriate methods. When the axial field is applied to Q0 in a tandem quadrupole set, it speeds passages of ions through Q0 and reduces delay caused by the need to refill Q0 with ions when jumping from low to high mass in Q1. When used as collision cell Q2, the axial field reduces the delay needed for daughter ions to drain out of Q2. The axial field can also be used to help dissociate ions in Q2, either by driving the ions forwardly against the collision gas, or by oscillating the ions axially within the collision cell. See Abstract

Thomson (250) also discloses that in many quadrupole mass spectrometers there are four rod sets, referred to as Q0, Q1, Q2 and Q3. Rod set Q0 receives ions

and gas from an ion source and has a radio frequency voltage (RF) only applied to it, to act as an ion transmission device while permitting gas therein to be pumped away. Rod set Q1 has RF and DC applied thereto, to act as a mass filter, e.g. to transmit a desired parent ion. Rod set Q2 has collision gas supplied thereto, to act as a collision cell for fragmentation of the parent ions, and typically has only RF applied thereto. Rod set Q3 has RF and DC applied thereto to act as a scannable mass filter for the daughter ions produced in collision cell Q2. See Column 1, line 19-29.

Thomson further discloses that appropriate RF and DC potentials are applied to opposed pairs of rods of the rod sets Q0 to Q3, and to the various ion optical elements 22, 28, 31b and 35b by a power supply 48 which is part of a controller indicated at 50. Appropriate DC offset voltages are also applied to the various rod sets by power supply 48. A detector 56 detects ions transmitted through the last set of rods Q3. In use, normally only RF is applied to rod set Q0 (via capacitors C1 from rod set Q1 to avoid the need for a separate power supply), plus a DC rod offset voltage which is applied uniformly to all the rods. This rod offset voltage delivers the electric potential inside the rod set (the axial potential). Because the rods have conductive surfaces, and the rod offset potential is applied uniformly to all four rods, the potential is constant throughout the length of the rod set, so that the electric field in an axial direction is zero (i.e. the axial field is zero). Rod set Q0 acts as an ion transmission device, transmitting ions axially therethrough while permitting gas entering rod set Q0 from orifice 31a to be pumped away. Therefore the gas pressure in rod set Q0 can be relatively high, particularly when chamber 18 is at atmospheric pressure and the

pressure in gas curtain chamber 24 is slightly above atmospheric. The gas pressure in rod set Q0 is in any event kept fairly high to obtain collisional focusing of the ions, e.g. it can be about 8 millitorr. By way of typical example, the offsets applied may be 1,000 volts DC on plate 22, 100 volts DC on plate 28, 0 volts on the skimmer 31b, and -20 to -30 volts DC offset on Q0 (this may vary depending on the ion being looked at). The rod offsets for Q1, Q2 and Q3 depend on the mode of operation, as is well known.

Rod set Q1 normally has both RF and DC applied to it, so that it acts as an ion filter, transmitting ions of desired mass (or in a desired mass range), as is conventional. Rod set Q2 has collision gas from a collision gas source 58 injected into its interior volume 42 and is largely enclosed in a grounded metal case 60, to maintain adequate gas pressure (e.g. 8 millitorr) therein. Rod set Q2 has RF only applied to it, plus (as mentioned) a rod offset voltage which defines the electric potential in the volume of the rod set. The rod offset voltage is used to control the collision energy in an MS/MS mode, where Q2 acts as a collision cell, fragmenting the parent ions transmitted into it through rod sets Q0 and Q1.

The daughter ions formed in the collision cell constituted by rod set Q2 are scanned sequentially through rod set Q3, to which both RF and DC are applied. Ions transmitted through rod set Q3, are detected by detector 56. The detected signal is processed and stored in memory and/or is displayed on a screen and printed out. See Column 5, line 5-55.

Thomson (250) still further discloses a quadrupole (Q-pole) mass spectrometer that includes RF quadrupole of rods divided into six sections, and the same amplitude

RF voltage applied to all sections. Such a segmented quadrupole was utilized as Q0 transmitting ions from an atmospheric pressure ion source 16 into Q1. When the voltage difference along the total length of the rods is zero volts, corresponding to no axial field, approximately 50 milliseconds are required for the ion signal to reach steady state. As the axial field is increased, the time to reach a steady state signal decreases, to about 10 milliseconds with V=5 volts. This corresponded to a gradient of about 5/6 volts per section. The axial field thus permits the use of Q0 at high pressure in a situation where the ions must be transmitted rapidly at steady state from one end of the RF quadrupole Q0 to the other. In this mode of operation several m/z values can be sequentially monitored at a rapid rate (i.e. 10 milliseconds per m/z value), and in which the RF quadrupole Q0 can transmit each m/z ion from the ion source to the entrance of Q1 with little delay. See Column 8, line 23-34, line 63-67; and Column 9, line 1-14.

Thomson (250) also discloses in FIG. 29, a high pressure entrance rod set 182 (functioning as Q0) which receives ions from an atmospheric pressure ion source 184. Rod set 182 is located in chamber 185 pumped by pump 186. Ions from source 184 are transmitted into Q0 through an opening 187, a gas curtain chamber 188, an aperture 189, a first stage vacuum chamber 190a pumped by pump 190b, and a skimmer orifice 191. From Q0, ions are directed through orifice 192 into a low pressure region 194 containing a pair of plates 196, 198, one of which (plate 198) is simply a wire grid. The low pressure region 194 is evacuated by a pump 200. In known fashion, ions in the low pressure volume 202 between plates 196, 198 may be

pulsed sideways, as a group, by suitable DC pulses, into a Time-of-Flight drift tube 204, at the end of which is located a detector 206. The axial velocity of ions in rod set Q0' can be controlled by applying DC axial potentials as described, in order to eliminate problems associated with fill and empty times of Q0. Control of the axial field also allows control of the timing of admission of ions into the volume 202 between plates 196, 198. Plates 196, 198 can also be formed as described to provide an axial DC field along their length, e.g. they can be segmented along their length, as indicated by segments 196-1 to 196-6 and 198-1 to 198-6, the segments being separated by insulating strips 199. Alternatively auxiliary rods (not shown) can be provided. By controlling the axial field so provided, ions entering the low pressure volume 202 between plates 196, 198 can be slowed to a stop in the axial direction and can then be pulsed sideways as a group down Time-of-Flight tube 204 for detection in conventional manner.

Since the Time-of-Flight system shown in FIG. 29 is a pulsed device, it may be advantageous to store ions in Q0 while one ion pulse is being analyzed (by for example, raising the potential on the exit plate), and then admit the next pulse of ions into the extraction plates 196, 198. An axial field in Q0 can be used to rapidly eject the ions into the extraction region when required so as to have a narrower pulse than would be available if the ions were simply to leak out due to space charge .

The plates 196, 198 may alternately be replaced by an RF quadrupole with rods 198a, 198b, 198c, 198d (FIG. 30) and with a slot 200 in one rod 198c, as described in the copending application of Charles Jolliffe entitled "Mass Spectrometer with Radial

Ejection". The RF rods in this region will confine the ions to a narrow radial position in space, and an axial field may be applied after admitting the ions, in order to slow them to a stop in the axial direction. After slowing the ions, or bringing them to rest, a voltage pulse may be applied to the opposite rod 198a in order to inject the ions through slot 200 into the flight tube for analysis. See Column 12, line 15-66.

In addition, it is well known in the art to produce mass separation using the Coulomb force generated by an electric field formed by four Q-poles of a mass spectrometer, as recited in Claims 15,20,21,31,38, and 43.

It is also implied herein that application of potentials to quadrupoles in accordance with Thomson (250) is equivalent to the use of Coulomb forces and space charge effects for mass separation as recited in Claims 15,20,25,31,38, and 43.

Thomson (250) also discloses that the axial field of the invention may also be used to alleviate the effects of fringing fields at the entrance and exit of Q1, wherein an axial field can be placed at the entrance and exit to speed up ions as they enter and leave Q1 but to slow down their passage through the center portion of Q1 so that they will undergo more oscillations in the resolving field, thereby increasing the resolution of Q1. This can be accomplished by providing a segmented case or auxiliary rods or electrodes 220 around the resolving or center portion of rods 222, and by adjusting the entrance and exit offsets to speed ions into and out of rod set 222 but adjusting the axial potential created by case or rods 220 to slow down ions during their passage through the center portion of rod set 222. See Column 14, line 28-45, and FIG. 32.

Thomson (250) further discloses a Quadrupole (Q-pole) mass spectrometer that includes quadrupole rod set where the RF applied equally to all the bands 158-1 to 158-5 is conducted to some extent through the resistive coatings on segments 160 to provide a relatively uniform RF field along the length of the rod 156. However with different DC voltages V1 to V5 applied to the bands, a DC voltage gradient is established along the length of the rod 156. Any desired gradient can be chosen, e.g. a gradient entirely in one direction to speed passage of ions through the rod set, or a gradient having a potential well at the center (lengthwise) of the rod set, for use in ion containment applications. See Column 11, line 21-32, and Figure 25.

It is implied herein that use of the resistive coatings as described above, are equivalent to the use of a "thin film" as recited in Claims 21 and 39.

Thomson (250) also teaches a quadrupole mass spectrometer, wherein the axial field in the presence of cooling gas, can be used to provide some separation of ions as they drift through the device under the action of the axial field, while the collisional focusing in the radial direction prevents ions from being lost by diffusion. For example, if ions are admitted into an RF multipole with an axial field, in the presence of cooling gas or drift gas, the ion velocity will reach a constant value, which is proportional to the axial field. Ions of different size will drift at different velocities dependant on their shape, mass and charge, and be separated in time when they reach the exit of the device. If the exit gate (e.g. a lens at exit orifice 192) is opened at an appropriate time, only ions of a certain type will be admitted in the following analyzing device or other detector such as a mass spectrometer. This mobility separation, may be applied to

assist in the analysis of a mixture of ions, where ions of the same or similar masses may have different drift times, thus adding an additional degree of specificity to the analysis. See Column 13, line 20-38.

In addition, it is well known in the art to utilize a magnetic field in mass spectrometers, wherein ion motion is "carried out using the Lorentz force", as recited in Claims 27 and 41.

2. Applicant's arguments filed 5-05-2003 have been fully considered but they are not persuasive.

3. Argument 1.

Applicant states that " as is clear from the Background of Thomson, as well as the discussion of the invention of Thomson, quadrupoles QO and Q2 do not subject the ions to mass separation. Rather, they are used for collisional focusing for Q 1 and Q3, respectively. And as is clear from the discussion; e.g., from Col. 6, 1-45, and col. 8, 1-23, etc., Thomson contemplates the invention for use with quadrupoles QO and Q2, and not Q 1 or Q3. Generally speaking, the point of the invention of Thomson is to reduce delay in the introduction of ions to Q 1 and Q3 by improving QO and Q2. There is no disclosure or suggestion of applying these concepts of Thomson to Ql or Q3.

The practical effect of this discussion of Thomson is to make it clear that Thomson does not, in fact, disclose or suggest controlling the axial motion of the ions while the ions are in the Q-pole region and undergoing mass separation as required by

each of claims 15 and 31. Claim 15 requires controlling the motion of the ions to be measured in the axial direction, advancing from the ion source to a collector, within the Q-pole region at the same time that the ions to be measured are subjected to mass separation in the Q-pole region by Coulomb force, etc. Claim 31 requires means for controlling the motion of the ions to be measured in the axial direction, advancing from the ion source toward the collector, at the same time that the ions to be measured are subjected to mass separation in the Q-pole region by Coulomb force, etc. In Thomson, the ions do not undergo mass separation in QO or Q 1. Accordingly, it may be seen that neither of the independent claims is disclosed or suggested by Thomson, and indication of such is respectfully requested."

The applicant is respectfully directed to Thomson (250), Column 5, line 36-38, which states; Rod set Q1 normally has both RF and DC applied to it, so that it acts as an ion filter, transmitting ions of desired mass (or in a desired mass range), as is conventional.

The examiner has interpreted from the Thomson (250) reference that the appropriate RF and DC potentials are applied to rod set Q1, so that mass separation of the ions (ion filtering) is provided in Q1 for the desired mass range in accordance with Thomson (250).

4. Argument 2

Applicant states that "Applicant specifically traverses the Examiner's positions that (1) it is well known in the art that a space charge can be used to control the motion of ions in the Q-pole region in a quadrupole mass spectrometer (2) that it is well known in the art to utilize a magnetic field in mass spectrometers wherein ion motion is carried out using Lorentz force."

Regarding space charge effects, the Applicant is respectfully directed to U.S. Patent No.'s 5,783,824 and 5,426,301.

Regarding the Lorentz force, the Applicant is also respectfully directed to U.S. Patent No.'s 6,182,831, and 4,931,640.

The examiner has interpreted from the references above that under appropriate application of RF and DC fields to the quadrupoles of a mass spectrometer, the positively charged ions inside the quadrupole set will repel each other with a normal Coulomb force, which is also known as the space charge effect .

5. In view of the corrections in the amendment dated 5-5-2003, the objection to the specification is hereby withdrawn.

Conclusion

6. The Amendment filed on 5-5-2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Thomson (250) reference.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip A Johnston whose telephone number is 305 7022. The examiner can normally be reached on 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John R Lee can be reached on 703 308 4116. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872 9318 for regular communications and 703 872 9319 for After Final communications.

JOHN R. LEE
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